

REMARKS

Figure 4 has been amended in the manner requested by the Examiner. The amendments do not introduce new matter within the meaning of 35 U.S.C. § 132. Accordingly, entry of the amendments is respectfully requested.

Interview with the Examiner

The courtesy extended by the Examiner during the interview with applicants' counsel on July 15, 1997 is appreciated.

In the interview, applicants' counsel presented the Examiner with proposed amendments to Figure 4 and formal drawings for the remaining Figures to overcome the outstanding objection to the drawings. The Examiner indicated that the proposed amendments and formal drawings appeared to overcome the outstanding objection.

As requested by the Examiner, applicants' counsel also agreed to resubmit the attachments to the Declaration previously submitted by the inventor, Dr. Britta Hardy, to the U.S. Patent and Trademark Office on February 27, 1997 (hereafter "the first Declaration").

In response to the outstanding rejection under 35 U.S.C. § 112, first paragraph, applicants' counsel offered to submit a supplemental Declaration by Dr. Hardy stating that the "BAT mAb" monoclonal antibody referred to in the first Declaration is identical to the BAT-1 mAb referred to in the application, and that

human tumors in immunodeficient mice (hereafter "human-mice xenograft models") are accepted in the relevant field as predictive of the activity of the BAT-1 mAb in humans. The Examiner acknowledged that such Declaration would, in most circumstances, overcome a § 112, first paragraph, rejection. To strengthen applicants' response, the Examiner suggested that applicants submit along with the supplemental Declaration by Dr. Hardy, additional Declarations by those of ordinary skill in the art or references supporting the acceptability of the human-mice xenograft models.

Objection to Drawings

The Examiner has maintained the objection to the drawings because the subfigures of Figures 1-4 are not separately labeled.

Applicants submit herewith proposed amendments to Figure 4, with the proposed amendments shown in red, for approval by the Examiner.

Applicants will submit formal drawings separately labeling the subfigures of Figures 1-3, as well as formal drawings for the remaining figures, upon indication of allowable subject matter by the Examiner.

Accordingly, applicants respectfully request the Examiner to reconsider and withdraw this objection.

Rejection of Claims 24-27 under 35 U.S.C. § 112, ¶ 1

Claims 24-27 have been rejected under 35 U.S.C. § 112, first paragraph, as not enabled for claims drawn to the *in vivo* treatment of human tumors by the administration of monoclonal antibodies.

As the basis of this rejection, the Examiner states:

A Declaration by Dr. Britta Hardy has been provided that documents anti-tumor activity of the "BAT mAb" monoclonal antibody in nude mice carrying xenografts of the human HT-29 colon carcinoma tumor cell line and in SCID mice engrafted with human lymphocytes and inoculated with human SK-28 melanoma tumor cells. The declaration also demonstrates the *in vitro* stimulatory effect of BAT mAb on human peripheral blood lymphocytes that were pre-incubated on monolayers of HT-28 human colon carcinoma tumor cells.

Clarification is requested. The claimed method is drawn to the use of the monoclonal antibody secreted by the hybridoma cell line CNCM Accession No. I-1397, which is called the BAT-1 monoclonal antibody (see specification p.7, lines 11-17). The declaration gives results obtained from the "BAT" monoclonal antibody. Given that in addition to the BAT-1 antibody the specification also discloses the BAT-2, BAT-4 and BAT-5 monoclonal antibodies (see Description of Figure 1, p.9), the question is raised as to whether the results set forth in the declaration were obtained with the same BAT-1 antibody of the claimed cancer treatment method.

If the "BAT" monoclonal antibody of the declaration is not the very same antibody as the "BAT-1" monoclonal, the declaration provides results irrelevant to the question at hand, and the rejection under 35 U.S.C. § 112, first paragraph, is maintained.

Further, assuming the identity of the "BAT" and the "BAT-1" monoclonal antibodies, the rejection under 35 U.S.C. § 112, first paragraph, is maintained. While the declaration documents the anti-tumor activity of the monoclonal antibody against the human HT-29 colon carcinoma tumor cell line in the nude mouse and the human SK-28 melanoma tumor cell line in the SCID mice, both are human xenografts into the mouse system. Hird and Epenetos notes that "nude mice containing human tumor

xenografts are the most widely used animal model. The data obtained from the mouse studies are useful, but cannot be directly translated to apply to the human situation" (see p.185). However, the record contains no evidence that such model systems are widely accepted by those of skill in the art to be predictive of the effectiveness of the claimed method in the treatment of human tumors and cancer.

Applicants submit herewith a supplemental Declaration by Dr. Britta Hardy, confirming that: (1) the "BAT mAb" monoclonal antibody referred to in the first Declaration is identical to the BAT-1 mAb referred to in the application; and (2) human-mice xenograft models are acceptable in the field of anti-cancer drug development for human use, as being predictive of the activity of BAT-1 mAb in humans.

Applicants further submit herewith five (5) abstracts of journal articles which exemplify the acceptability of the human-mice xenograft models.

As requested by the Examiner, applicants also resubmit Attachments A and B (Curriculum Vitae and List of Publications, respectively) of the first Declaration originally submitted by Dr. Hardy on February 27, 1997.

Accordingly, applicants respectfully request the Examiner to reconsider and withdraw this objection.

Withdrawal of Previously Raised Objections and Rejections

Applicants acknowledge with appreciation the Examiner's withdrawal of the objections to the disclosure; the rejection of claims 19-27 under 35 U.S.C. § 112, first paragraph, as lacking complete deposit information; the rejection of claims 19-27 under 35 U.S.C. § 112, first paragraph, as not being enabled; the rejection of claims 20 and 24-27 under 35 U.S.C. § 112, second paragraph; and the rejection of claims 19, 21-22, 24 and 26 under 35 U.S.C. § 102(b).

CONCLUSION

Based upon the above amendments and remarks, the presently claimed subject matter is believed to be novel and patentably distinguishable over the prior art of record. Accordingly, the Examiner is respectfully requested to reconsider and withdraw the rejections of claims 24-27 and allow all pending claims presented herein for reconsideration.

The Examiner is welcomed to telephone the undersigned attorney
if she has any questions or comments.

Respectfully submitted,

NATH & ASSOCIATES

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